UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,732	09/26/2007	Michael D. Dake	13720-10507IUS2	3155

65989 7590 09/15/2011

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
09/15/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,732	DAKE ET AL.	
	Examiner	Art Unit	
	LaKia Tongue	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *51,53-55,64-73,77-117,146 and 149-151* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *51,53-55,64-73,77-117,146 and 149-151* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/20/11 & 6/13/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's supplemental response filed on June 13, 2011 is acknowledged. Claims 52, 56-63, 74-76 and 118-145 have been canceled. Claim 151 has been added. Claims 51, 53, 86, 87, 92-96, 104 and 108 have been amended. Claims 51, 53-55, 64-73, 77-117, 146 and 149-151 are pending and under examination.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on May 20, 2011 and June 13, 2011 are in compliance with the provisions of 37 CFR 1.97 and have been considered. An initialed copy is attached hereto.

Objections Withdrawn

3. In view of Applicant's amendment, the objection to the specification because the application failed to comply with the requirements of 37 C.F.R. 1.821-1.825 because it contains sequences that are not identified is withdrawn.

4. In view of Applicant's amendment, the objection to the specification for the use of the trademarks NeutrAvidin (page 24) and Cetaphil (page 32) have been withdrawn.

5. In view of Applicant's amendment, the objection to claim 53 because the word "in" following "51" needs to be deleted is withdrawn.

6. In view of Applicant's amendment, the objection to the claims for failure to comply with the requirements of 37 C.F.R. 1.821-1.825 because it contains sequences that are not identified is withdrawn.

7. In view of Applicant's amendment, the objection to claims 52 and 108 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn.

Rejections Withdrawn

8. In view of Applicants cancellation of claim 118, the rejection of claims 51 and 116-118 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention by the use of the phrase "cell-encapsulating device" is withdrawn.

9. In view of Applicant's amendment, the rejection of claim 104 for lacking antecedent basis for the limitation "in which the polyalkyleneimine is a polyethyleneimine" is withdrawn.

10. In view of Applicant's argument (the reference is not available as prior art because the inventors are the same), the rejection of claims 51-55, 64-73, 77-118, 146, 149 and 150 under 35 U.S.C. 102(e) as being anticipated by Waugh et al. (U.S. 2004/0220100 A1; filing date: 7/21/00) is withdrawn.

11. In view of Applicant's argument (the reference is not available as prior art because the inventors are the same), the rejection of claims 51-55, 77, 80, 81, 86-93, 97-104, 110-115 and 118 under 35 U.S.C. § 102(e) as being anticipated by Waugh et al. (US 2003/0229034 A1; filing date: 6/21/01) is withdrawn.

12. In view of Applicant's argument (the reference is not available as prior art because the inventors are the same), the rejection of claims 64-73, 78, 79, 82-85, 94-96, 105-109, 116, 149 and 150 under 35 U.S.C. 103(a) as unpatentable over Waugh et al. (US 2003/0229034 A1; filing date: 6/20/01) as applied to claims 51-55, 77, 80, 81, 86-93, 97-104, 110-115 and 118 above in view of Hanin (U.S. Patent No. 6,688,311 B2; filing date: 3/14/02) is withdrawn.

13. In view of Applicant's argument (the reference is not available as prior art because the inventors are the same), the rejection of claim 117 under 35 U.S.C. 103(a) as unpatentable over Waugh et al. (U.S. 2003/0229034 A1; filing date: 6/20/01), Hanin (U.S. Patent No. 6,688,311 B2; filing date: 3/14/02) as applied to claims 51-55, 64-73, 77-116, 118, 149 and 150 above, and further in view of Waugh et al. (U.S. 2004/0220100 A1; filing date: 7/21/00) is withdrawn.

Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. The rejection of claims 51, 53-55, 64-73, 77-93, 97, 110, 149 and 150 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 78-80, 88 and 90-97 of copending Application No. 10/591,485 ('485); PG Pub 2008/0200373 A1 is maintained for the reasons set forth in the previous office action.

Applicant request that said rejection be held in abeyance since the pending application is still under prosecution. Applicants reserve the right to file a terminal disclaimer or to amend the claims should it become necessary at a later stage of prosecution.

Applicant's request has been considered and the rejection will be maintained until Applicant has either submitted a terminal disclaimer or has amended the claims to obviate said rejection.

As previously presented, although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the '485 claims are drawn to a method of topically applying to the skin or epithelium of a subject, a composition comprising a carrier which has a polymeric backbone having positively charged branching groups and a biologically active protein, wherein the carrier and the biologically active protein associate non-covalently. The biologically active protein of the '485 application is a botulinum toxin.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. The rejection of claims 51, 54, 55, 77, 80-87, 97, 98, 149 and 150 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10 and 11 of copending Application No. 12/647,677 ('677) is maintained for the reasons set forth in the previous office action.

Applicant request that said rejection be held in abeyance since the pending application is still under prosecution. Applicants reserve the right to file a terminal disclaimer or to amend the claims should it become necessary at a later stage of prosecution.

Applicant's request has been considered and the rejection will be maintained until Applicant has either submitted a terminal disclaimer or has amended the claims to obviate said rejection.

As previously presented, although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the '677 claims are drawn to a method of administering botulinum toxin to achieve a therapeutic or cosmetic effect to an individual in need thereof comprising administering a composition comprising a positively charged carrier comprising a charged backbone, wherein the positively charged carrier is non-covalently associated with the botulinum toxin. Moreover, claim 10 of the '677 application recites that the treatment is for wrinkles, which one of ordinary skill in the art would considered a topical application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 51, 53-55, 86-101, 110-115 and 151 are rejected under 35 U.S.C. 102(b) as being anticipated by Waugh et al. (WO 02/07773 A2; Published: 1/31/02).

Independent claim 51 is drawn to a method of administering a botulinum toxin to a subject comprising topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged efficiency groups, wherein the botulinum toxin is not covalently modified and wherein the carrier and the botulinum toxin non-covalently and directly associate.

Waugh et al. disclose a method for administering compositions which are useful for the delivery of therapeutic agents (see abstract). Said compositions comprise a

variety of biological agents, which include both therapeutic and cosmetic agents. Suitable cosmetic agents include Botulinum toxin (Botox) (see page 15, lines 20, 21, 26, 27, 33 and 34). The present invention provides compositions comprising a non-covalent association complex of a positively-charged backbone having at least one attached efficiency group and at least one nucleic acid member (see page 17, lines 27-30). Waugh et al. disclose that said compositions can be formulated to provide mixtures for topical administration to the skin. They may be in sterile, isotonic solutions, which include the addition of sterilized water or of physiological saline (page 19, lines 4-7). Preferably, the formulation will be about 5% to 75% by weight of a composition of the invention (see page 20, lines 1-3). Moreover, the formulations can take the form of solid, semi-solid, or liquid dosage forms, for example, creams, ointments, lotions and gels (see page 20, lines 7-10 and page 21, line 6). In some embodiments, a sustained-release formulation can be administered (see page 20, lines 19-20).

Waugh et al. disclose that the positively charged backbone is a polypeptide having branching efficiency groups comprising $(Gly)_{n1}$-$(Arg)_{n2}$, HIV-TAT or fragments thereof, in which the subscript n1 is an integer of from 0 to 20, and subscript n2 is an odd integer of from 5 to 25. Waugh et al. further disclose that said positively charged backbone and groups are a polypeptide having the formula $(gly)_p$-RGRD-DRRQRR-$(gly)_q$ or $(gly)_p$-YGRKKRRQRRR-$(gly)_q$ (see page 9, lines 5-15). Waugh et al. disclose that the positively charged backbone is a polylysine having a molecular weight of 70,000 to 150,000 and 150,000 to 300,000 (see page 9, lines 17-23).

Applicant's arguments are addressed below regarding the use of Waugh.

Applicant argues that:

1) Waugh '773 does not anticipate or render obvious the presently pending claims because Waugh does not disclose "any method of administering botulinum toxin to a subject" in which "the carrier and the botulinum toxin non-covalently and directly associate", as required by the claims.

2) To the extent that Waugh mentions botulinum toxin, it requires it to be covalently attached to a negatively charged backbone (page 10, lines 15-17).

3) Example 4 does not render the presently claimed invention obvious and simply shows that a protein can be functionalized by negative charges distributed directly on the protein.

4) By contrast, the presently claimed invention concerns botulinum toxin rather than insulin.

Applicant's arguments have been considered, but are deemed non-persuasive.

With regard to Points 1 and 3, as outlined above, Waugh et al. disclose a method of administering a botulinum toxin to a subject comprising topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged efficiency groups, wherein the botulinum toxin is not covalently modified and wherein the carrier and the botulinum toxin non-covalently and directly associate (see page 15, lines 20, 21, 26, 27, 33 and 34; page 17, lines 27-30; and page 19, lines 4-7). While

Waugh does not provide specific examples of its use for botulinum toxin, the disclosure of Waugh fully anticipates the instantly claimed invention.

With regard to Point 2, Waugh et al. do not specifically disclose that the botulinum toxin is required to be covalently attached to a negatively charged backbone as Applicant argues. Further, Waugh does not exclude the biological agent, in this instance botox, from having a positively charged backbone present. In fact, Waugh et al. specifically disclose that the present invention provides compositions comprising a non-covalent association complex of a positively-charged backbone having at least one attached efficiency group and at least one nucleic acid member (see page 17, lines 27-30).

With regard to Point 4, while Example 4 pertains to insulin, Waugh specifically discloses that in the most preferred embodiment, the biological agent is selected from insulin, botulinum toxin and 4 others. Consequently, botulinum toxin is equivalent to insulin and the specification teaches specific modifications to the biological agents, which are identical to those limitations of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 51, 53-55, 64-73, 77-101, 109-117, 146 and 149-151 rejected under 35 U.S.C. 103(a) as being unpatentable over Waugh et al. (WO 02/07773 A2; Published: 1/31/02), and further in view of First (U.S. 2011/0206731 A1; Filed 12/9/03).

Independent claim 51 is drawn to a method of administering a botulinum toxin to a subject comprising topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged efficiency groups, wherein the botulinum toxin is not covalently modified and wherein the carrier and the botulinum toxin non-covalently and directly associate.

Dependent claim 64 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the face of the subject, or to a portion thereof.

Dependent claim 65 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the axilla of the subject, or to a portion thereof.

Dependent claim 66 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the palms of the hands or to the feet of the subject, or to a portion thereof.

Dependent claim 67 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the back or neck of the subject, or to a portion thereof.

Dependent claim 68 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the groin of the subject, or to a portion thereof.

Dependent claim 69 is drawn to the method of claim 51 in which the composition is applied topically to the hands or feet of the subject, or to a portion thereof.

Dependent claim 70 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the elbows, upper arms, knees, or upper legs of the subject, or to a portion thereof.

Dependent claim 71 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the buttocks of the subject, or to a portion thereof.

Dependent claim 72 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the torso of the subject, or to a portion thereof.

Dependent claim 73 is drawn to the method of claim 51 in which the botulinum toxin is applied topically to the pelvis, or to a portion thereof.

Dependent claim 77 is drawn to the method according to claim 51 in which the botulinum toxin is a botulinum toxin derivative.

Dependent claim 78 is drawn to the method of claim 51 in which the botulinum toxin comprises a recombinant botulinum toxin.

Dependent claim 79 is drawn to the method of claim 51 in which the botulinum toxin comprises a modified botulinum toxin.

Dependent claims 80-85, 149 and 150 are drawn to the method of claim 51 in which the botulinum toxin is selected from botulinum toxin serotypes A, B, C, D, E, F and G (clm 80); A (81), B (82), C (83), D (84), E (85), F(149) and G (150).

Dependent claim 109 is drawn to the method according to claim 51 in which the botulinum toxin is applied in a composition having a pH of from about 4.5 to about 6.3.

Dependent claim 116 is drawn to the method of claim 51 in which the botulinum toxin is contained in a device for dispensing the botulinum toxin, which device is applied topically to the skin or epithelium of the subject.

Dependent claim 117 is drawn to the method of claim 116 in which the device is a skin patch.

Dependent claim 146 is drawn to the method according to claim 51 in which the botulinum toxin comprises a fusion protein.

Waugh et al. disclose a method for administering compositions which are useful for the delivery of therapeutic agents (see abstract). Said compositions comprise a variety of biological agents, which include both therapeutic and cosmetic agents. Suitable cosmetic agents include Botulinum toxin (Botox) (see page 15, lines 20, 21, 26, 27, 33 and 34). The present invention provides compositions comprising a non-covalent association complex of a positively-charged backbone having at least one attached efficiency group and at least one nucleic acid member (see page 17, lines 27-30). Waugh et al. disclose that said compositions can be formulated to provide mixtures for topical administration to the skin. They may be in sterile, isotonic solutions, which include the addition of sterilized water or of physiological saline (page 19, lines 4-7). Preferably, the formulation will be about 5% to 75% by weight of a composition of the invention (see page 20, lines 1-3). Moreover, the formulations can take the form of solid, semi-solid, or liquid dosage forms, for example, creams, ointments, lotions and gels (see page 20, lines 7-10 and page 21, line 6). In some embodiments, a sustained-release formulation can be administered (see page 20, lines 19-20).

Waugh et al. disclose that the positively charged backbone is a polypeptide having branching efficiency groups comprising $(Gly)_{n1}$-$(Arg)_{n2}$, HIV-TAT or fragments thereof, in which the subscript n1 is an integer of from 0 to 20, and subscript n2 is an odd integer of from 5 to 25. Waugh et al. further disclose that said positively charged backbone and groups are a polypeptide having the formula $(gly)_p$-RGRD-DRRQRR-$(gly)_q$ or $(gly)_p$-YGRKKRRQRRR-$(gly)_q$ (see page 9, lines 5-15). Waugh et al. disclose that the positively charged backbone is a polylysine having a molecular weight of 70,000 to 150,000 and 150,000 to 300,000 (see page 9, lines 17-23).

Waugh et al. do not specifically disclose the claim limitations of claims 64-73 and 77-85 as recited above.

First discloses methods for treating skin disorders by local administration of botulinum toxin to a patient with a skin disorder (see abstract). The method can be carried out by administration of a botulinum toxin types A, B, C, D, E, F, or G to a patient by a transdermal route, which includes application of said toxin in a cream, suspension, gel, emulsion, imbedded in a patch applied to the skin or in a lotion as a vehicle (see paragraph 0054). First discloses that the use of botulinum toxin is for the treatment of disorders and/or a cosmetically undesirable state or condition in an individual, such as various skin pigment disorders, noncancerous disorders, dermatofibromas, dermoid cyst, freckles, keloids, keratoacanthomas, lipomasmoles (nevi), atypical moles (dysplastic nevi), pyogenic granulomas, seborrheic keratoses, actinic keratosis, and skin tags by applying an amount of a therapeutically effective dose of botulinum toxin topically, via transdermal patch (see paragraphs 0058 and

0068). Therefore, the Examiner has interpreted said affliction to potentially have a location anywhere on the human body. More specifically, First discloses that the botulinum toxin can be applied to regions of the foot (paragraph 0098; Example 4), regions of the face and neck (paragraphs 0100, 0103 & 0104; Examples 6, 9 & 10), regions of the leg and arm (paragraph 0102; Example 8), as well as both axillae (paragraph 0106; Example 12). Lastly, First discloses that said toxin may be recombinantly made, hybrid, modified and chimeric (see paragraph 0060).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Waugh et al. to topically administer the botulinum toxin to the particular body parts as claimed and recited above; to use the serotypes A-G, and/or use modified, chimeric or recombinant botulinum toxins as taught by First because of the many benefits and advantages associated with said toxin, such as the ability for the symptoms of a skin disorder to be dramatically reduced or eliminated; the ability to have the symptoms reduced or eliminated for at least about two weeks to about six months per administration of said toxin; few or no significant undesirable side effects occur from administration of said toxin and the administration of said toxin can result in the desirable side effects of greater patient mobility, a more positive attitude, and an improved quality of life (see First; paragraphs 0108-0113).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the composition to different areas of the skin as recited because both Waugh et al. and First disclose topical administration of botulinum toxin to the skin, which includes the face, axilla, palms of the hands, feet, neck, elbows,

arms, knees, and torso. While First does not specifically recite the groin, buttocks or pelvis, all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. See the recent Board decision *Ex parte Smith,--USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

Moreover, regarding the specific pH of the composition as recited in claim 109, MPEP 2144.05 states, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14

USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler,* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)."

Limitations such as a pH of a particular component are being viewed as limitations of optimizing experimental parameters.

One would have had a reasonable expectation, barring evidence to the contrary, that the composition, since all components are known to be used for the same or similar reasons, would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

18. Claims 102-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waugh et al. (WO 02/07773 A2; Published: 1/31/02) and First (U.S. 2011/0206731 A1; Filed 12/9/03) as applied to claims 51, 53-55, 64-73, 77-101, 109-117, 146 and 149-151 above, and further in view of Swann (U.S. Patent 4,434,228; Published: 2/28/84).

Independent claim 51 is drawn to a method of administering a botulinum toxin to a subject comprising topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged efficiency groups, wherein the botulinum toxin is not covalently modified and wherein the carrier and the botulinum toxin non-covalently and directly associate.

Dependent claim 102 is drawn to the method according to claim 51 in which the backbone comprises a positively charged nonpeptidyl carrier.

Dependent claim 103 is drawn to the method according to claim 102 in which the positively charged nonpeptidyl polymer is polyalkyleneimine.

Dependent claim 104 is drawn to the method according to claim 103 in which the polyalkyleneimine is a polyethyleneimine.

Dependent claim 105 is drawn to the method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

Dependent claim 106 is drawn to the method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.

Dependent claim 107 is drawn to the method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

Dependent claim 108 is drawn to the method according to claim 102 in which the botulinum toxin comprises a recombinant botulinum toxin.

The limitations of Waugh et al. and First have been set forth supra.

The combination of Waugh et al. and First do not specifically disclose the limitations of claims 102-108 as defined above.

Swann discloses an invention which produces an insolubilized biological material composite which contains biological materials entrapped within a condensed polyalkyleneimine polymer (see column 1, lines 55-58). Swann discloses that the polyalkyleneimines generally vary between 30,000 and 100,000 in molecular weight, depending on reaction conditions. Lastly, Swann discloses that polyethyleneimine (PEI) is a preferred polyalkyleneimine, because it is currently readily available at relatively low cost and it functions well in the condensation reactions (see column 2, lines 49-59).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Waugh et al. and First to have the backbone comprise a positively charged nonpeptidyl carrier because such composites exhibit excellent strength and durability (see Swann-column 1, lines 62-63). Additionally, it is obvious to have the backbone comprise a positively charged polyethyleneimine because it is readily available at a relatively low cost and it functions well in condensation reactions (see Swann-column 2, lines 56-59).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a positively charged nonpeptidyl carrier, particularly polyalkyleneimine or polyethyleneimine because all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. See the recent Board decision *Ex parte Smith,--USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

Regarding claim 107, limitations such the molecular weight of a particular component are being viewed as limitations of optimizing experimental parameters.

One would have had a reasonable expectation, barring evidence to the contrary, that the method of administering a botulinum toxin to a subject would have yielded predictable and effective results to one of ordinary skill in the art at the time of the invention.

Conclusion

19. No claim is allowed.

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Suskind et al. (US 2005/0074466 A1).

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LaKia Tongue whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
8/30/11

/VANESSA L FORD/
Primary Examiner, Art Unit 1645